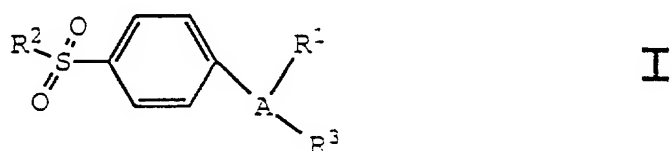


What is claimed is :

1. A method to suppress immune, acute or delayed-type hypersensitivity response in a subject, said method comprising treating the subject with a therapeutically-effective amount of a 5-lipoxygenase inhibitor and a cyclooxygenase-2 inhibitor selected from Dupont Dup 697, Taisho NS-398, meloxicam, flosulide and compounds of Formula I



wherein A is a 5- or 6-member ring substituent selected from partially unsaturated or unsaturated heterocyclo and carbocyclic rings;

wherein R<sup>1</sup> is at least one substituent selected from heterocyclo, cycloalkyl, cycloalkenyl and aryl, wherein R<sup>1</sup> is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

wherein R<sup>2</sup> is selected from alkyl, and amino; and

wherein R<sup>3</sup> is a radical selected from halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocycloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclo, cycloalkenyl, aralkyl, heterocycloalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl,

alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-aryl-amino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-aryl-amino, aminoalkyl, alkylaminoalkyl, N-aryl-aminoalkyl, N-aralkylaminoalkyl, N-alkyl-N-aralkylaminoalkyl, N-alkyl-N-aryl-aminoalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-arylaminosulfonyl, arylsulfonyl, N-alkyl-N-arylaminosulfonyl;

10 or a pharmaceutically-acceptable salt thereof.

2. The method of Claim 1 wherein said 5-lipoxygenase inhibitor and said cyclooxygenase-2 inhibitor are administered in a sequential manner.

3. The method of Claim 1 wherein said 5-lipoxygenase inhibitor and said cyclooxygenase-2 inhibitor are administered in a substantially simultaneous manner.

4. The method of Claim 1 wherein the 5-lipoxygenase inhibitor is selected from masoprocrol, tenidap, zileuton, flobufen, lonapalene, tagorizine, Abbott A-121798, Abbott A-76745, N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N'-hydroxyurea (Abbott A-78773), (R)(+)N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N-hydroxyurea (Abbott A-79175), Abbott ABT 761, Dainippon AL-3264, Bayer Bay-x-1005, Biofor BF-389, bunaprolast, Cytomed CMI-392, Takeda CV-6504, Efamol EF-40, Ciba-Geigy CGS-26529, enazadrem phosphate, Leo Denmark ETH-615, flezelastine hydrochloride, lonapalene, Merck Frosst L 663536, Merck Frosst L 699333, Merckle ML-3000, 3M Pharmaceuticals R-840, rilopirox, Schering Plough SCH 40120, tepoxalin, linazolast (TMK-688), Tanabe T-757, Tanabe T-799, Zeneca ZD 7717, Zeneca ZM-216800, Zeneca ZM 230487, and Zeneca ZD-2138.

5. The method of Claim 4 wherein the 5-lipoxygenase inhibitor is selected from tenidap, zileuton, flobufen, lonapalene, tagorizine, Abbott A-121798, Abbott A-76745, N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N'-hydroxyurea (Abbott A-78773), (R)(+)-N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N'-hydroxyurea (Abbott A-79175), Abbott ABT 761, Ciba-Geigy CGS-26529, Biofor BF-389, Cytomed CMI-392, Leo Denmark ETH-615, lonapalene, Merck Frosst L 699333, Merckle ML-3000, 3M Pharmaceuticals R-840, linazolast (TMK-688), Tanabe T-757, Tanabe T-799, Zeneca ZD 7717, Zeneca ZM-216800, Zeneca ZM 230487, and Zeneca ZD-2138.

6. The method of Claim 1 wherein A is selected from oxazolyl, isoxazolyl, dihydrofuryl, imidazolyl, and pyrazolyl; wherein R<sup>1</sup> is selected from 5- and 6-membered heterocyclo, and aryl selected from phenyl, biphenyl and naphthyl, wherein R<sup>1</sup> is optionally substituted at a substitutable position with one or more radicals selected from lower alkyl, lower haloalkyl, cyano, carboxyl, lower alkoxy carbonyl, hydroxyl, lower hydroxyalkyl, lower haloalkoxy, amino, lower alkylamino, phenylamino, nitro, lower alkoxyalkyl, lower alkylsulfinyl, halo, lower alkoxy and lower alkylthio; wherein R<sup>2</sup> is amino; and wherein R<sup>3</sup> is a radical selected from oxo, cyano, carboxyl, lower alkoxy carbonyl, lower carboxyalkyl, lower cyanoalkyl, halo, lower alkyl, lower alkyloxy, lower cycloalkyl, phenyl, lower haloalkyl, 5- or 6-membered heterocyclo, lower hydroxylalkyl, lower aralkyl, acyl, phenylcarbonyl, lower alkoxyalkyl, 5- or 6-membered heteroaryloxy, aminocarbonyl, lower alkylaminocarbonyl, lower alkylamino, lower aminoalkyl, lower alkylaminoalkyl, phenyloxy, and lower aralkoxy; or a pharmaceutically-acceptable salt thereof.

7. The method of Claim 6 wherein A is selected from oxazolyl, isoxazolyl, imidazolyl, and pyrazolyl; wherein R<sup>1</sup> is phenyl optionally substituted at a substitutable position with one or more radicals selected from methyl, ethyl, isopropyl, butyl, *tert*-butyl, isobutyl, pentyl, hexyl, trifluoromethyl, cyano, carboxyl, methoxycarbonyl, hydroxyl, hydroxymethyl, trifluoromethoxy, amino, N-methylamino, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, nitro, methoxymethyl, methylsulfinyl, fluoro, chloro, bromo, methoxy, ethoxy, propoxy, *n*-butoxy, pentoxy, and methylthio; wherein R<sup>2</sup> is amino; and wherein R<sup>3</sup> is a radical selected from oxo, cyano, carboxyl, methoxycarbonyl, ethoxycarbonyl, carboxypropyl, carboxymethyl, carboxyethyl, cyanomethyl, fluoro, chloro, bromo, methyl, ethyl, isopropyl, butyl, *tert*-butyl, isobutyl, pentyl, hexyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, fluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, methoxy, ethoxy, propoxy, *n*-butoxy, pentoxy, cyclohexyl, phenyl, pyridyl, thienyl, thiazolyl, oxazolyl, furyl, pyrazinyl, hydroxylmethyl, hydroxylpropyl, benzyl, formyl, phenylcarbonyl, methoxymethyl, furylmethoxy, aminocarbonyl, N-methylaminocarbonyl, N,N-dimethylaminocarbonyl, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, aminomethyl, N,N-dimethylaminomethyl, N-methyl-N-ethylaminomethyl, benzyloxy, and phenyloxy; or a pharmaceutically-acceptable salt thereof.

8. The method of Claim 7 selected from compounds, their prodrugs and their pharmaceutically-acceptable salts, of the group consisting of

3-(3,4-difluorophenyl)-4-(4-methylsulfonylphenyl)-  
2-(5H)-furanone;

3-phenyl-4-(4-methylsulfonylphenyl)-2-(5H)-furanone;

5 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-  
pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-  
pyrazol-1-yl]benzenesulfonamide;

10 4-[5-(3-fluoro-4-methoxyphenyl)-3-  
(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

3-[1-[4-(methylsulfonyl)phenyl]-4-trifluoromethyl-  
1H-imidazol-2-yl]pyridine;

2-methyl-5-[1-[4-(methylsulfonyl)phenyl]-4-  
trifluoromethyl-1H-imidazol-2-yl]pyridine;

15 4-[2-(5-methylpyridin-3-yl)-4-(trifluoromethyl)-  
1H-imidazol-1-yl]benzenesulfonamide;

4-[5-methyl-3-phenylisoxazol-4-  
yl]benzenesulfonamide;

20 4-[5-hydroxyethyl-3-phenylisoxazol-4-  
yl]benzenesulfonamide;

[2-trifluoromethyl-5-(3,4-difluorophenyl)-4-  
oxazolyl]benzenesulfonamide;

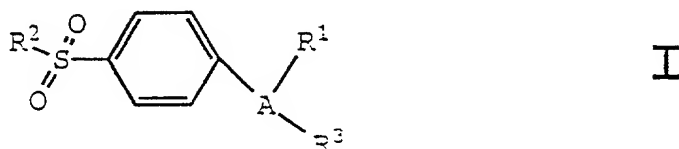
4-[2-methyl-4-phenyl-5-  
oxazolyl]benzenesulfonamide; and

25 4-[5-(3-fluoro-4-methoxyphenyl)-2-trifluoromethyl)-  
4-oxazolyl]benzenesulfonamide.

9. A combination comprising a therapeutically-  
effective amount of a cyclooxygenase-2 inhibitor, a 5-  
30 lipxygenase inhibitor and an immunosuppressive drug  
selected from antiproliferative agents,  
antiinflammatory-acting compounds and inhibitors of  
leukocyte activation.

35 10. The combination of Claim 9 wherein the  
cyclooxygenase-2 inhibitor is selected from Dupont Dup-

697, Taisho NS-398, meloxicam, flosulide and compounds of Formula I



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wherein A is a 5- or 6-member ring substituent selected from partially unsaturated or unsaturated heterocyclo and carbocyclic rings;

wherein R<sup>1</sup> is at least one substituent selected from heterocyclo, cycloalkyl, cycloalkenyl and aryl, wherein R<sup>1</sup> is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

wherein R<sup>2</sup> is selected from alkyl, and amino; and

wherein R<sup>3</sup> is a radical selected from halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocycloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclo, cycloalkenyl, aralkyl, heterocycloalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-arylaminalkyl, N-aralkylaminalkyl, N-alkyl-N-aralkylaminalkyl, N-alkyl-N-arylaminalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-

arylaminosulfonyl, arylsulfonyl, N-alkyl-N-arylaminosulfonyl;

or a pharmaceutically-acceptable salt thereof.

- 5           11. The combination of Claim 9 wherein the 5-lipoxygenase inhibitor is selected from masoprocol, tenidap, zileuton, flobufen, lonapalene, tagorizine, Abbott A-121798, Abbott A-76745, N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N'-
- 10 hydroxyurea (Abbott A-78773), (R)(+)N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N-hydroxyurea (Abbott A-79175), Abbott ABT 761, Dainippon
- 15 AL-3264, Bayer Bay-x-1005, Biofor BF-389, bunaprolast, Cytomed CMI-392, Takeda CV-6504, Efamol EF-40, enazadrem phosphate, Leo Denmark ETH-615, flezelastine
- 20 hydrochloride, Merck Frosst L 663536, Merckle ML-3000, 3M Pharmaceuticals R-840, rilopirox, Schering Plough SCH 40120, tepoxalin, linazolast (TMK-688), Tanabe T-757, Tanabe T-799, Zeneca ZD-2138, Abbott A 72694,
- 25 Abbott A-80263, Biofor BF-397, Bristol-Myers Squibb BU-4601A, carbazoycin C, lagunamycin, Wellcome BW-70C, Ciba-Geigy CGS-26529, Warner-Lambert CI 1004, Warner-Lambert PD-136005, Warner-Lambert PD-145246, Eisai E 3040, Fujirebio F-1322, Fisons FPL-64170, Fujisawa FR
- 30 110302, Nippon Hypox HX 0386, Merck & Co L-699333, Merck Frosst L 739010, Lilly LY-269415, Lilly LY 178002, Meiji Milk MM-7002, Hoechst Roussel P 8892, Hoechst Roussel P 8977, SmithKline Beecham SB-202235, Green Cross SS-81-OH, Terumo Keio University TMK 685,
- 35 American Home Products WAY-121520, American Home Products WAY-125007, Zeneca ZD 7717, Zeneca ZM-216800, Zeneca ZM 230487, 1,2-dihydro-n-(2-thiazolyl)-1-oxopyrrolo(3,2,1-kl)phenothiazine-1-carboxamide, Abbott A-65260, Abbott A-69412, Abbott Abbott-63162, American
- Home Products AHR-5333, Bayer Bay-q-1531, Boehringer Ingelheim BI-L-357, Boehringer Ingelheim BI-L-93BS, Boehringer Ingelheim BIL 226XX, Bristol-Myers Squibb

5 BMY-30094, carbazomycin B, Wellcome BW 4C, Wellcome BW-  
 B218C, Wellcome BW-B70C, Chauvin CBS-1114, Ciba-Geigy  
 CGS-21595, Ciba-Geigy CGS-22745, Ciba-Geigy CGS-23885,  
 Ciba-Geigy CGS 24891, Ciba-Geigy CGS-8515, Chiesi CHF-  
 1909, Warner-Lambert CI-986, Warner-Lambert CI 987,  
 cirsilinol, docebenone, DuPont Merck DuP-654, Eisai E  
 5110, Eisai E-6080, Green Cross EN-105, enofelast,  
 epocarbazolin-A, eprovafen, evandamine, forsythiaside,  
 10 Fisons FPL 62064, Glaxo GR-80907, Zeneca ICI-211965,  
 isoflavans, Kyowa Hakko KF-8940, Merck & Co L-651392,  
 Merck & Co L-651896, Merck & Co L-652343, Merck & Co  
 L-656224, Merck & Co L-670630, Merck & Co L-674636,  
 Merck & Co L-691816, Lilly LY-233569, Lilly LY-280810,  
 Merck & Co MK-591, Merck & Co MK-886, nitrosoxacin-A,  
 15 Ono ONO-5349, Ono ONO-LP-219, Ono ONO-LP-269, Warner-  
 Lambert PD-127443, Purdue Frederick PF-5901, Sandoz QA-  
 208-199, Johnson & Johnson R-68151, Johnson & Johnson  
 R-85355, Rhone-Poulenc Rorer Rev-5367, Rhone-Poulenc  
 Rorer RG-5901-A, Rhone-Poulenc Rorer RG-6866, Roussel-  
 20 Uclaf RU-46057, Searle SC-41661A, Searle SC-45662,  
 Sandoz SDZ-210-610, SmithKline Beecham SK&F-104351,  
 SmithKline Beecham SK&F-104493, SmithKline Beecham  
 SK&F-105809, Synthelabo SL-81-0433, Teijin TEI-8005,  
 Terumo TMK-777, Terumo TMK-781, Terumo TMK-789, Terumo  
 25 TMK-919, Terumo TMK-992, Teikoku Hormone TZI-2721,  
 Teikoku Hormone TZI-41127, American Home Products WAY-  
 120739, American Home Products WY 47288, American Home  
 Products Wy-48252, American Home Products Wy-50295, and  
 Yoshitomi Y-19432.

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12. The combination of Claim 11 wherein the 5-  
 lipooxygenase inhibitor is selected from masoprocol,  
 tenidap, zileuton, flibuifen, lonapalene, tagorizine,  
 Abbott A-121798, Abbott A-76745, N'-[[5-(4-  
 35 fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N'-  
 hydroxyurea (Abbott A-78773), (R)(+)N'-[[5-(4-  
 fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N-



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nitro, lower alkoxyalkyl, lower alkylsulfinyl, halo, lower alkoxy and lower alkylthio; wherein  $R^2$  is selected from lower alkyl and amino; and wherein  $R^3$  is a radical selected from halo, lower alkyl, oxo, cyano, carboxyl, lower cyanoalkyl, heteroaryloxy, lower alkyloxy, lower cycloalkyl, phenyl, lower haloalkyl, 5- or 6-membered heterocyclo, lower hydroxylalkyl, lower aralkyl, acyl, phenylcarbonyl, lower alkoxyalkyl, heteroaryloxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, alkylamino, aminoalkyl, alkylaminoalkyl, aryloxy, and aralkoxy; or a pharmaceutically-acceptable salt thereof.

15. The combination of Claim 14 wherein A is selected from oxazolyl, isoxazolyl, dihydrofuryl, imidazolyl, and pyrazolyl; wherein  $R^1$  is selected from 5- and 6-membered heterocyclo, and aryl selected from phenyl, biphenyl and naphthyl, wherein  $R^1$  is optionally substituted at a substitutable position with one or more radicals selected from lower alkyl, lower haloalkyl, cyano, carboxyl, lower alkoxycarbonyl, hydroxyl, lower hydroxyalkyl, lower haloalkoxy, amino, lower alkylamino, phenylamino, nitro, lower alkoxyalkyl, lower alkylsulfinyl, halo, lower alkoxy and lower alkylthio; wherein  $R^2$  is amino; and wherein  $R^3$  is a radical selected from oxo, cyano, carboxyl, lower alkoxycarbonyl, lower carboxyalkyl, lower cyanoalkyl, halo, lower alkyl, lower alkyloxy, lower cycloalkyl, phenyl, lower haloalkyl, 5- or 6-membered heterocyclo, lower hydroxylalkyl, lower aralkyl, acyl, phenylcarbonyl, lower alkoxyalkyl, 5- or 6-membered heteroaryloxy, aminocarbonyl, lower alkylaminocarbonyl, lower alkylamino, lower aminoalkyl, lower alkylaminoalkyl, phenyloxy, and lower aralkoxy; or a pharmaceutically-acceptable salt thereof.

16. The combination of Claim 15 wherein A is selected from oxazolyl, isoxazolyl, imidazolyl, and pyrazolyl; wherein R<sup>1</sup> is phenyl optionally substituted at a substitutable position with one or more radicals selected from methyl, ethyl, isopropyl, butyl, tert-butyl, isobutyl, pentyl, hexyl, trifluoromethyl, cyano, carboxyl, methoxycarbonyl, hydroxyl, hydroxymethyl, trifluoromethoxy, amino, N-methylamino, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, nitro, methoxymethyl, methylsulfinyl, fluoro, chloro, bromo, methoxy, ethoxy, propoxy, n-butoxy, pentoxy, and methylthio; wherein R<sup>2</sup> is amino; and wherein R<sup>3</sup> is a radical selected from oxo, cyano, carboxyl, methoxycarbonyl, ethoxycarbonyl, carboxypropyl, carboxymethyl, carboxyethyl, cyanomethyl, fluoro, chloro, bromo, methyl, ethyl, isopropyl, butyl, tert-butyl, isobutyl, pentyl, hexyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, fluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, methoxy, ethoxy, propoxy, n-butoxy, pentoxy, cyclohexyl, phenyl, pyridyl, thienyl, thiazolyl, oxazolyl, furyl, pyrazinyl, hydroxylmethyl, hydroxylpropyl, benzyl, formyl, phenylcarbonyl, methoxymethyl, furylmethoxy, aminocarbonyl, N-methylaminocarbonyl, N,N-dimethylaminocarbonyl, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, aminomethyl, N,N-dimethylaminomethyl, N-methyl-N-ethylaminomethyl, benzyloxy, and phenyloxy; or a pharmaceutically-acceptable salt thereof.

17. The combination of Claim 16 selected from compounds, their prodrugs and their pharmaceutically-acceptable salts, of the group consisting of

3-(3,4-difluorophenyl)-4-(4-methylsulfonylphenyl)-  
2-(5H)-furanone;

3-phenyl-4-(4-methylsulfonylphenyl)-2-(5H)-furanone;

4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-  
5 pyrazol-1-yl]benzenesulfonamide;

4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-  
pyrazol-1-yl]benzenesulfonamide;

4-[5-(3-fluoro-4-methoxyphenyl)-3-  
(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;

10 3-[1-[4-(methylsulfonyl)phenyl]-4-trifluoromethyl-  
1H-imidazol-2-yl]pyridine;

2-methyl-5-[1-[4-(methylsulfonyl)phenyl]-4-  
trifluoromethyl-1H-imidazol-2-yl]pyridine;

4-[2-(5-methylpyridin-3-yl)-4-(trifluoromethyl)-  
15 1H-imidazol-1-yl]benzenesulfonamide;

4-[5-methyl-3-phenylisoxazol-4-  
yl]benzenesulfonamide;

4-[5-hydroxyethyl-3-phenylisoxazol-4-  
yl]benzenesulfonamide;

20 [2-trifluoromethyl-5-(3,4-difluorophenyl)-4-  
oxazolyl]benzenesulfonamide;

4-[2-methyl-4-phenyl-5-  
oxazolyl]benzenesulfonamide; and

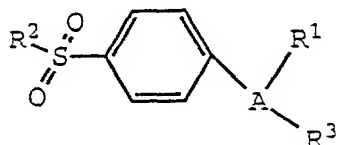
4-[5-(3-fluoro-4-methoxyphenyl)-2-trifluoromethyl)-  
25 4-oxazolyl]benzenesulfonamide.

18. The composition of Claim 9 wherein the  
leukocyte activation inhibitor is a cyclosporin.

30 19. The composition of Claim 18 wherein the  
cyclosporin is cyclosporin A.

20. A pharmaceutical composition comprising a  
pharmaceutically-acceptable carrier and a  
35 therapeutically-effective amount of a 5-lipoxygenase  
inhibitor, a cyclosporin and a cyclooxygenase-2

inhibitor selected from Dupont Dup 697, Taisho NS-398, meloxicam, flosulide and compounds of Formula I



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wherein A is a 5- or 6-member ring substituent selected from partially unsaturated or unsaturated heterocyclo and carbocyclic rings;

wherein R<sup>1</sup> is at least one substituent selected from heterocyclo, cycloalkyl, cycloalkenyl and aryl, wherein R<sup>1</sup> is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

wherein R<sup>2</sup> is selected from alkyl, and amino; and

wherein R<sup>3</sup> is a radical selected from halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocycloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclo, cycloalkenyl, aralkyl, heterocycloalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-arylaminalkyl, N-aralkylaminalkyl, N-alkyl-N-aralkylaminalkyl, N-alkyl-N-arylaminalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-

arylaminosulfonyl, arylsulfonyl, N-alkyl-N-arylaminosulfonyl;

or a pharmaceutically-acceptable salt thereof.

- 5           21. The method of Claim 1 further characterized  
by suppressing immune response in a subject susceptible  
to or afflicted with rejection of an organ transplanted  
to said subject; graft versus host disease; an  
autoimmune disease, an inflammatory disease, or a  
10 condition with underlying autoimmune or inflammatory  
reactivities or responses; an allergy; asthma; airway  
hypersensitivity; septic shock; myesthemia gravis;  
autoimmune thyroiditis; Grave's disease; autoimmune  
hemolytic anemia; autoimmune thromboeytopenia purpura;  
15 mixed connective tissue disease; idiopathic Addison's  
disease; Sjogren's syndrome; urticaria; an acute  
hypersensitivity response or a delayed hypersensitivity  
response; Goodpasture's syndrome; hemolytic anemia;  
contact dermatitis; granuloma; antibody-induced  
20 thrombocytopenia; hypersensitivity pneumonitis;  
glomerulonephritis; thyroiditis; encephalomyelitis; or  
meningitis.